Armed Forces College of Medicine

AFCM

Physiology of Endocrine Pancreas (2)

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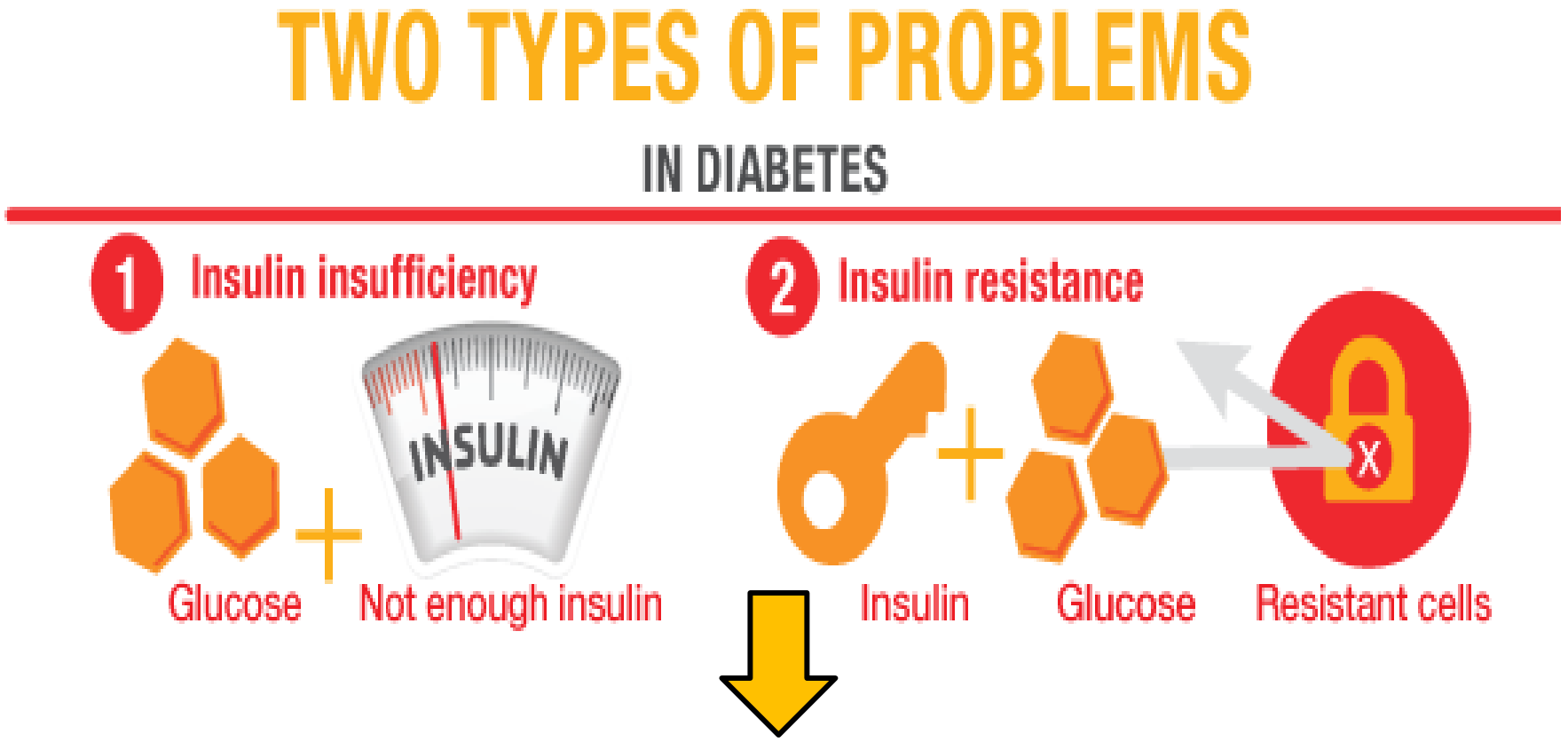
INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

1. Explain the consequences of deficient insulin secretion or insulin action.
2. List the physiological effects of glucagon.
3. Enumerate factors that regulate glucagon secretion.
4. Describe the physiologic effects of somatostatin in the pancreas.
5. List the anti-insulin hormones.
6. Summarize the hormones that affect the plasma glucose

Consequences of Insulin Deficiency

- The constellation of abnormalities caused by insulin deficiency is called **diabetes mellitus** which is due to a deficiency of the effects of insulin at the tissue level.



Consequences of Insulin Deficiency

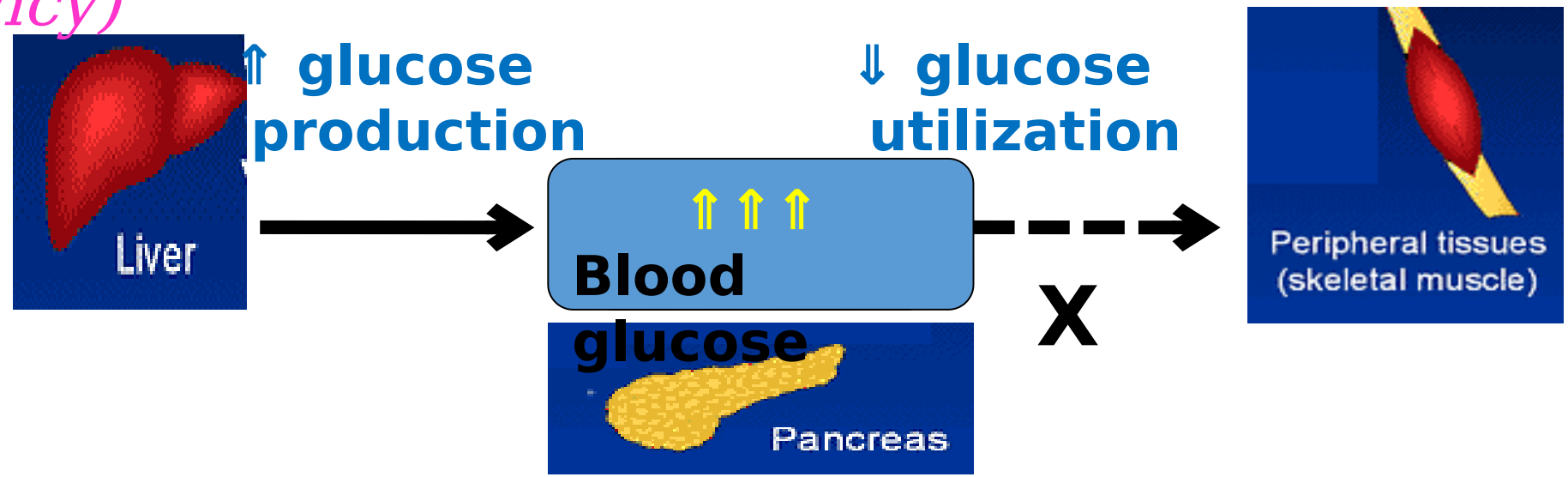
	Juvenile diabetes =Type I = IDDM	Maturation onset diabetes = Type II = NIDDM
1- Age of onset:	Occurs in **children** (<20 years).	Occurs in **adulthood** (> 40 years).
2- Incidence:	Account for **10-20%** of all cases	Account for **80-90%** of all cases
3- Cause:	**Total or partial lack of insulin secretion** due to autoimmune destruction of beta cells.	Inability of cells to respond to insulin released from the pancreas **(insulin resistance),** due to down regulation of insulin receptors.
4- Family history:	**-ve** family history (rare)	**+ve** family history

Consequences of Insulin Deficiency

I. Hyperglycemia:

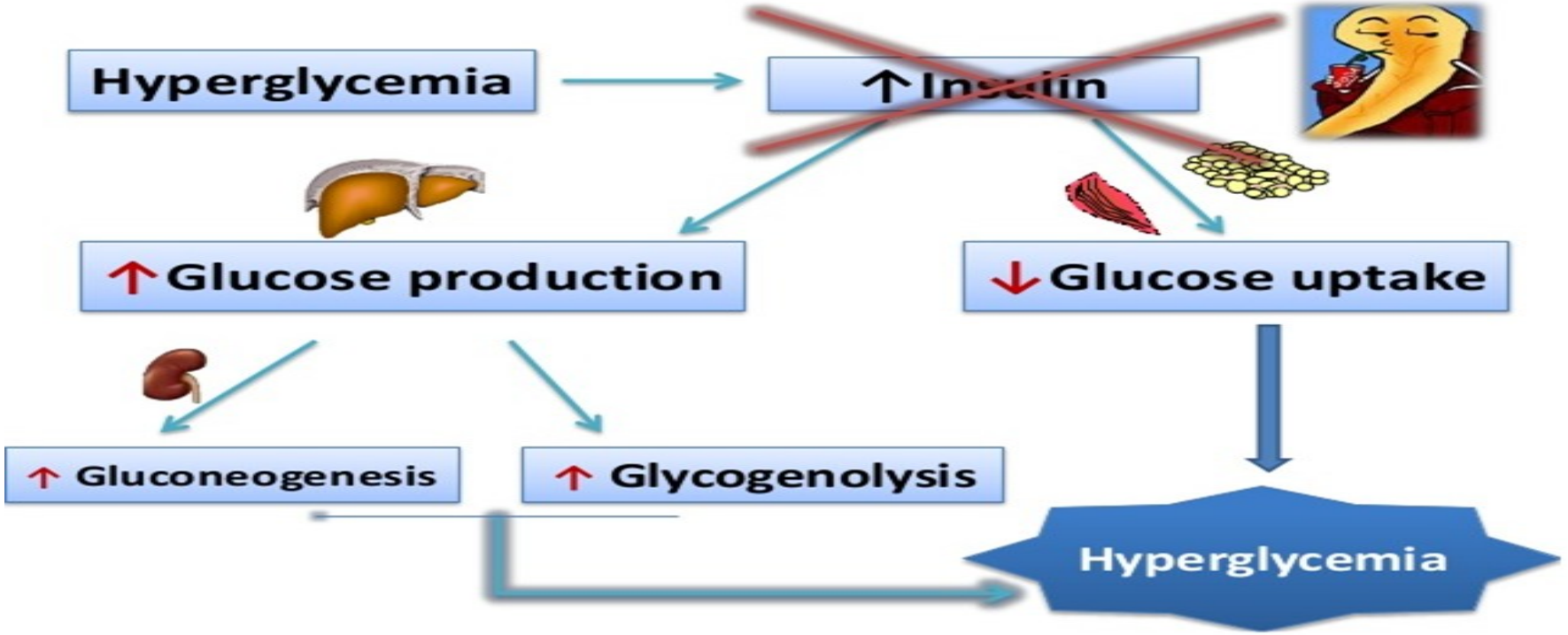
Due to decreased peripheral glucose utilization by cells & increased hepatic glucose output

(extracellular glucose excess + intracellular glucose deficiency)



Impaired insulin secretion or

Causes of hyperglycemia in DM:



I. **<u>Decreased peripheral glucose disposal (uptake) by muscles &adipose tissue due to</u>:** Lack of insulin.

<u>II. Increased hepatic glucose output due to:</u>

1- Enhanced gluconeogensis (↑ lipolysis glycerol & catabolism amino acids)

2- Enhanced glycogenolysis.

3- Increased glucagon.

Consequences of Insulin Deficiency

Effects of Hyperglycemia:

1. Polyuria (passage of large volumes of urine)

Hyperglycemia glucosuria (as the renal capacity for glucose reabsorption is exceeded) excretion of the osmotically active glucose molecules loss of large amounts of water (osmotic diuresis).

2. Polydipsia (excessive drinking)

Dehydration 2ry to osmotic diuresis activates the mechanisms regulating water intake polydipsia.

3. Polyphagia (increased appetite)

Due to decreased glucose uptake by satiety center so feeding center is not inhibited.

Consequences of Insulin Deficiency

Effects of Hyperglycemia:

4. Weight loss.

For every gram of glucose excreted, 4.1 kcal is lost from the body +……..??

5. ↑ HbA_{Ic}

When plasma glucose is elevated over time, small amounts of hemoglobin A are non

enzymatically glycated to form HbA_{Ic}

6. Recurrent infections.

7. **Long-term complications of diabetes** e.g retinopathy, nephropathy & peripheral neuropathy.

Consequences of Insulin Deficiency

II. Changes in protein metabolism:

(-) protein synthesis, **protein depletion** and wasting.

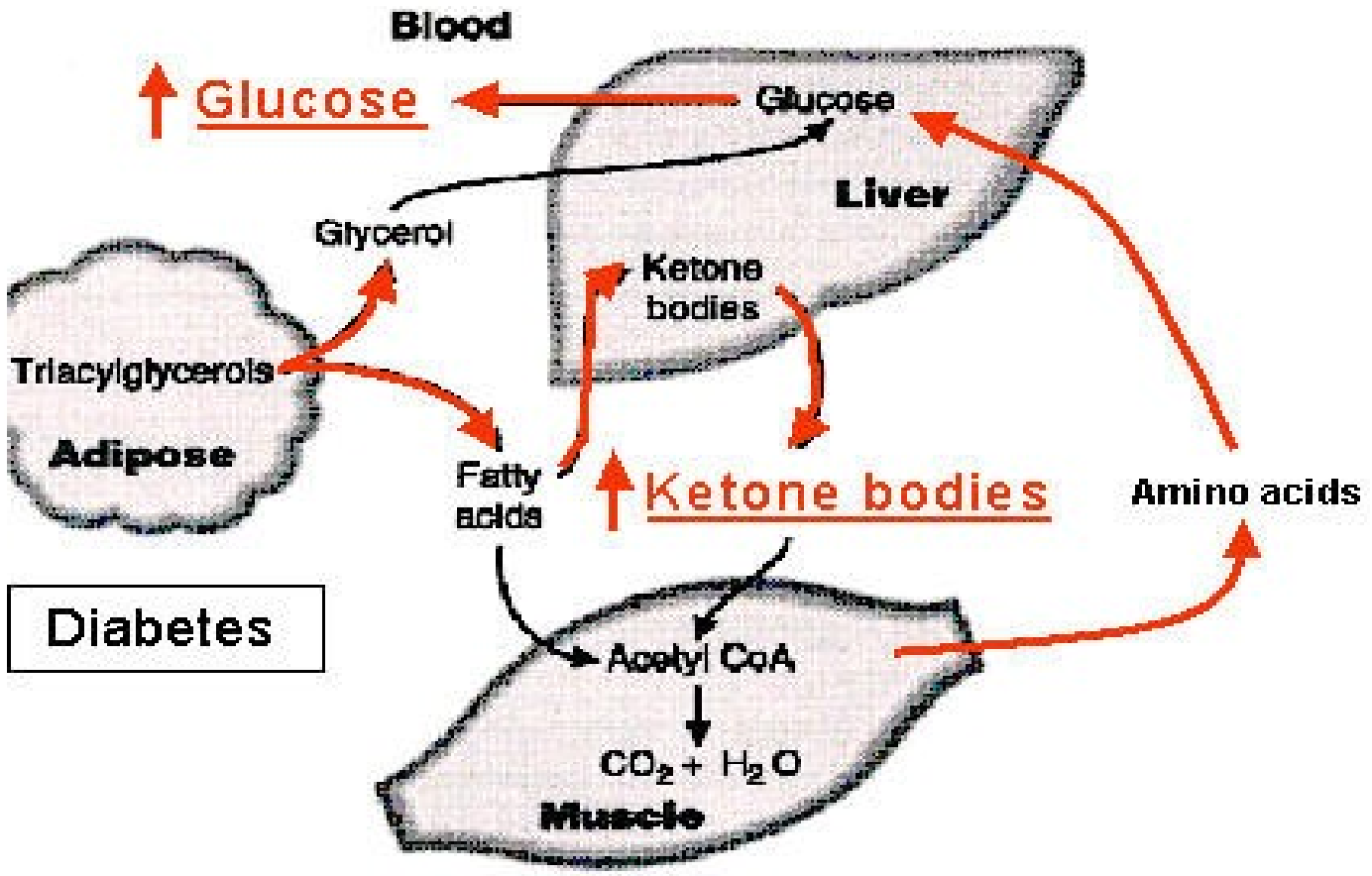
because, in the absence of insulin ↓ less protein synthesis occurs in muscle ↓ ↓ the supply of amino acids for gluconeogenesis

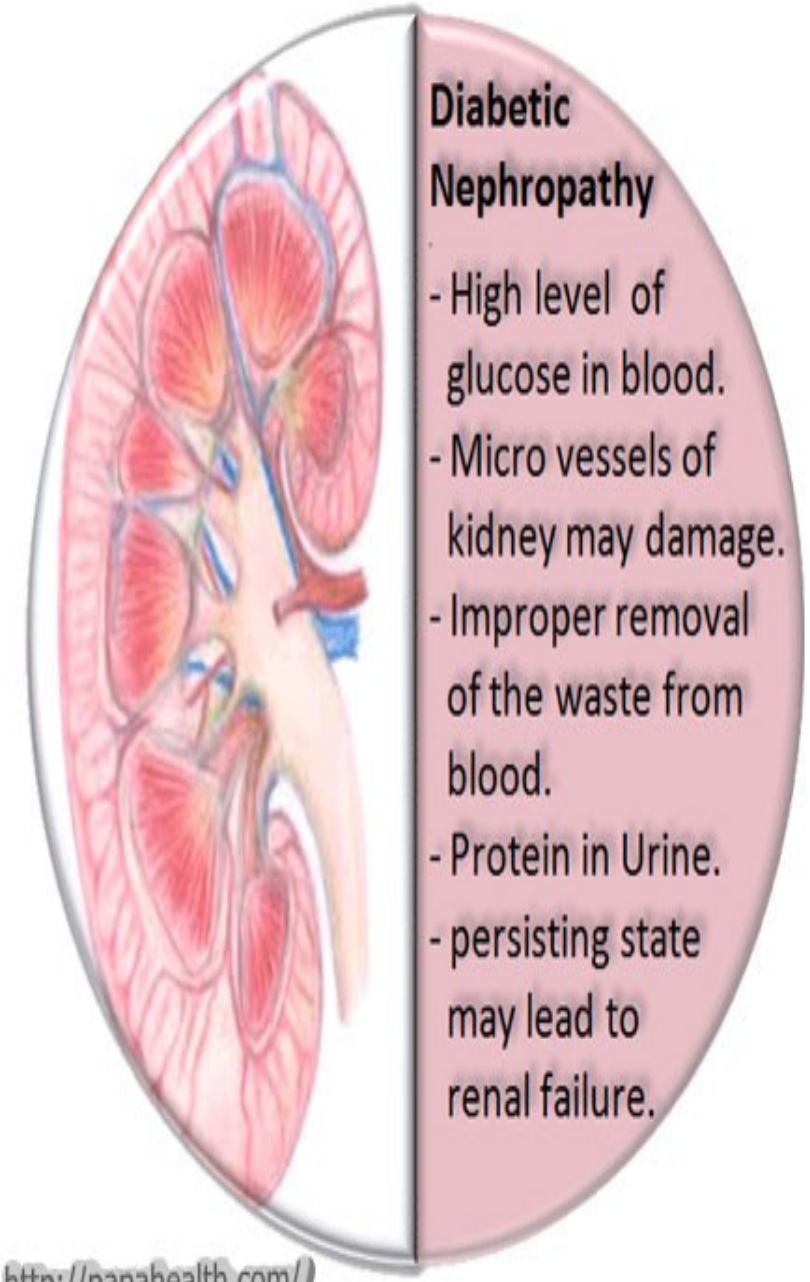
III: Changes in fat metabolism:

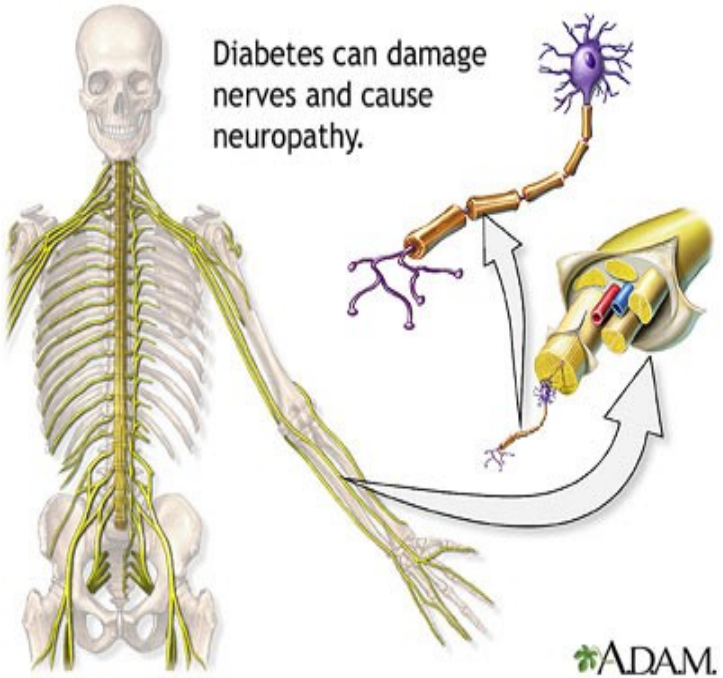
(-) synthesis of fatty acids and triglycerides, acceleration of lipid catabolism, with increased formation of ketone bodies,

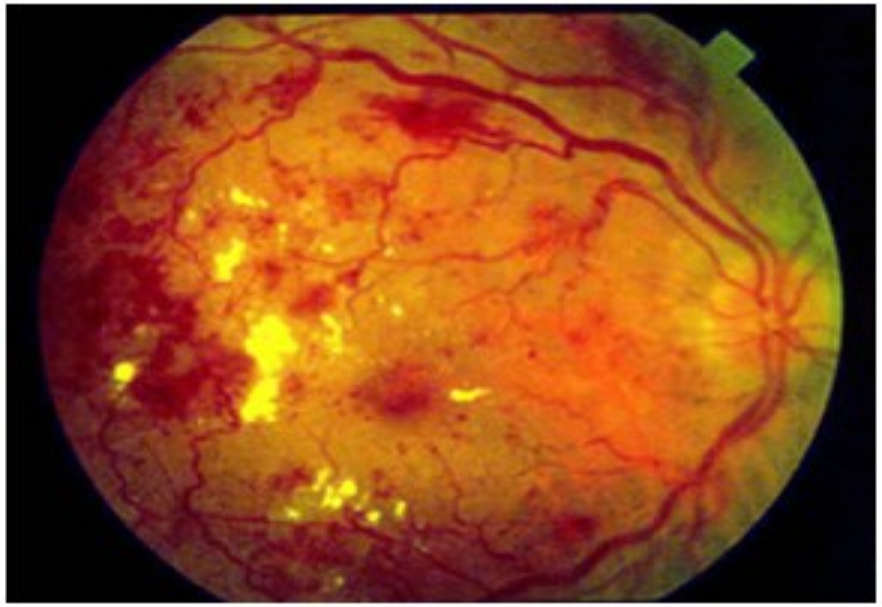
because in absence of insulin ↓ ↓ hormone-sensitive lipase ↑ (+) **lipolysis** ↑ ↑ free fatty acids levels ↑ catabolized in liver ↑ ↑ acetyl-

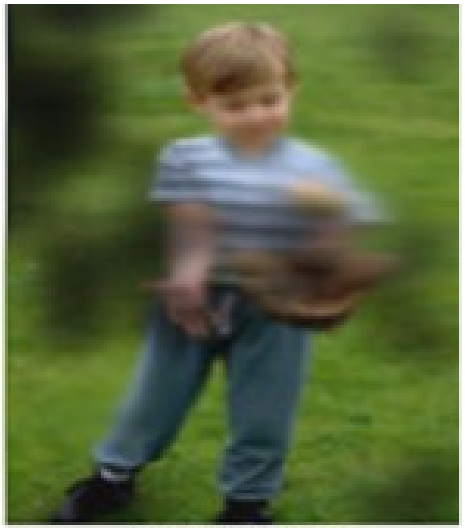
Energy metabolism, untreated diabetes











Normal vision

Vision with diabetic retinopathy

Glucagon Hormone

- **Site of release:**

  Alpha cells of the islets of Langerhans in response to falling levels of blood glucose.

- **Nature:**

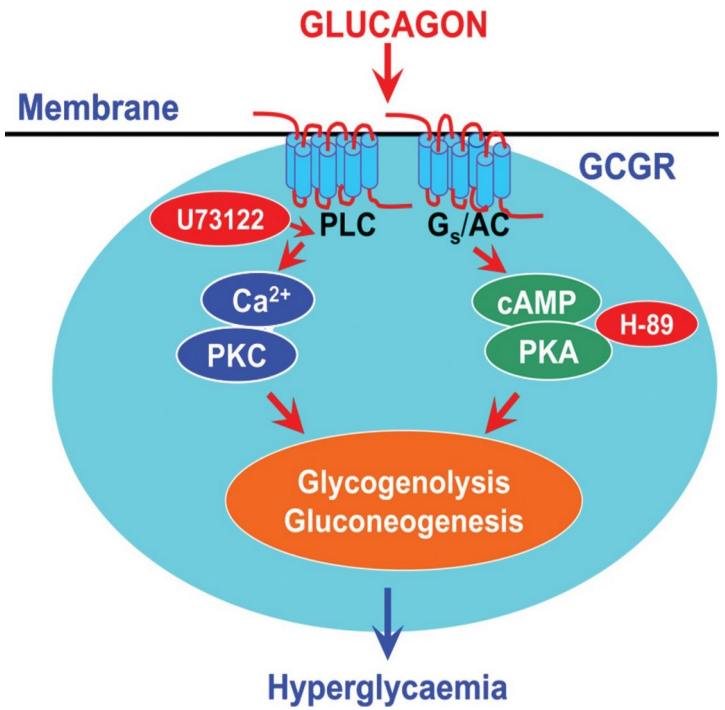
  Peptide hormone (29 a.a).

- **Mechanism of action:**

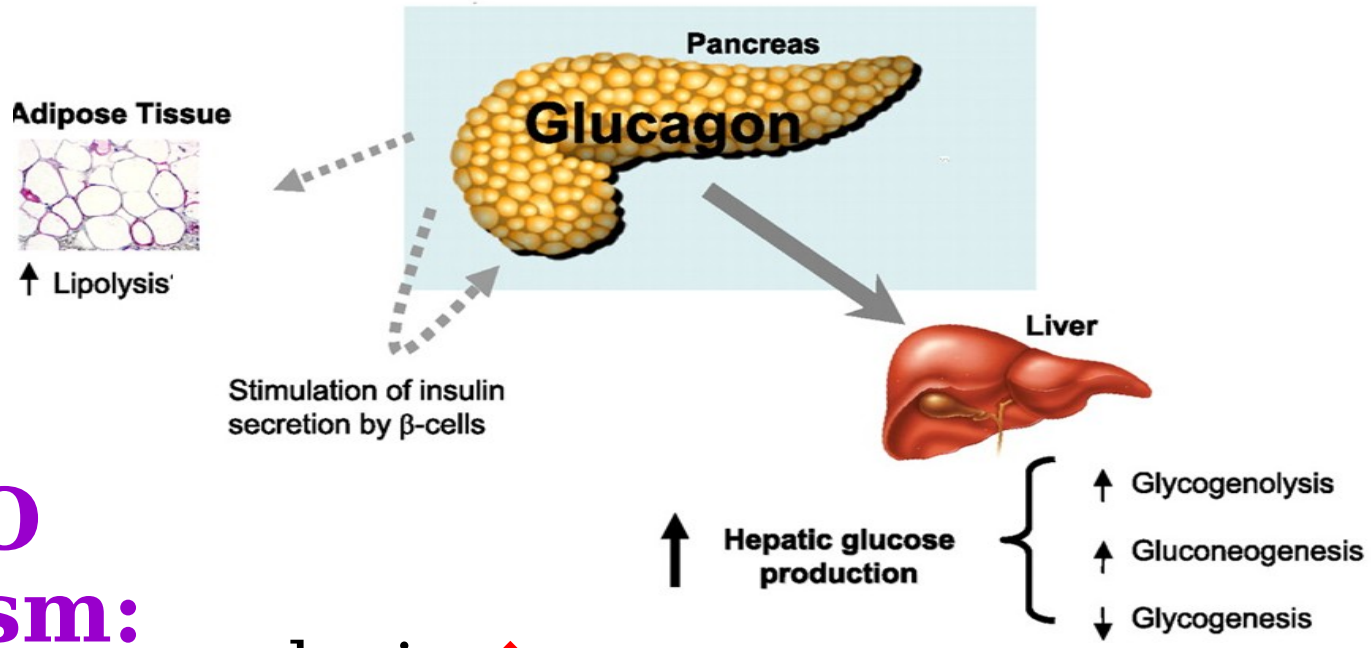
  Hydrophilic hr act via G protein coupled receptors ↑ cAMP.

- **Physiological actions:** are opposite to those of insulin

It is a hyperglycemic, lipolytic and catabolic hormone.



Glucagon Hormone



I. On CHO metabolism:

Hepatic glycogenolysis ↑

↑ gluconeogenesis **(How?)**

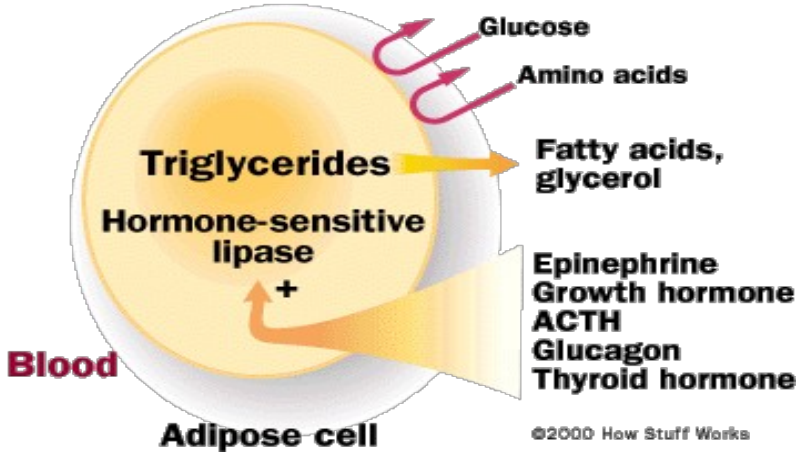
Amino acid transport into liver → ↑ gluconeogenesis ↑ -1

Lipolysis (TG → glycerol → ↑ gluconeogenesis) ↑ -2

So it is a hyperglycemic hormone

Glucagon Hormone

II. On fat metabolism:



https://science.howstuffworks.com/life/cellular-microscopic/fat-cell3.htm

- ↑ **Lipolysis** → ↑ blood fatty acid & glycerol.
  - Glycerol → substrate for gluconeogenesis.
  - Fatty acids → production of ketones (ketogenesis)

III. On protein metabolism:

- ↓ protein synthesis and ↑ protein c

.So it is a lipo

.The released amino acids are used for

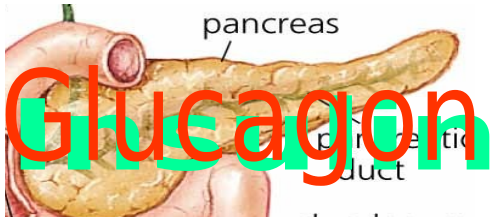
- **Calorigenic action**
- **+ve inotropic**
- **++ Secretion of insulin& Somatostatin.**

Regulation of glucagon secretion

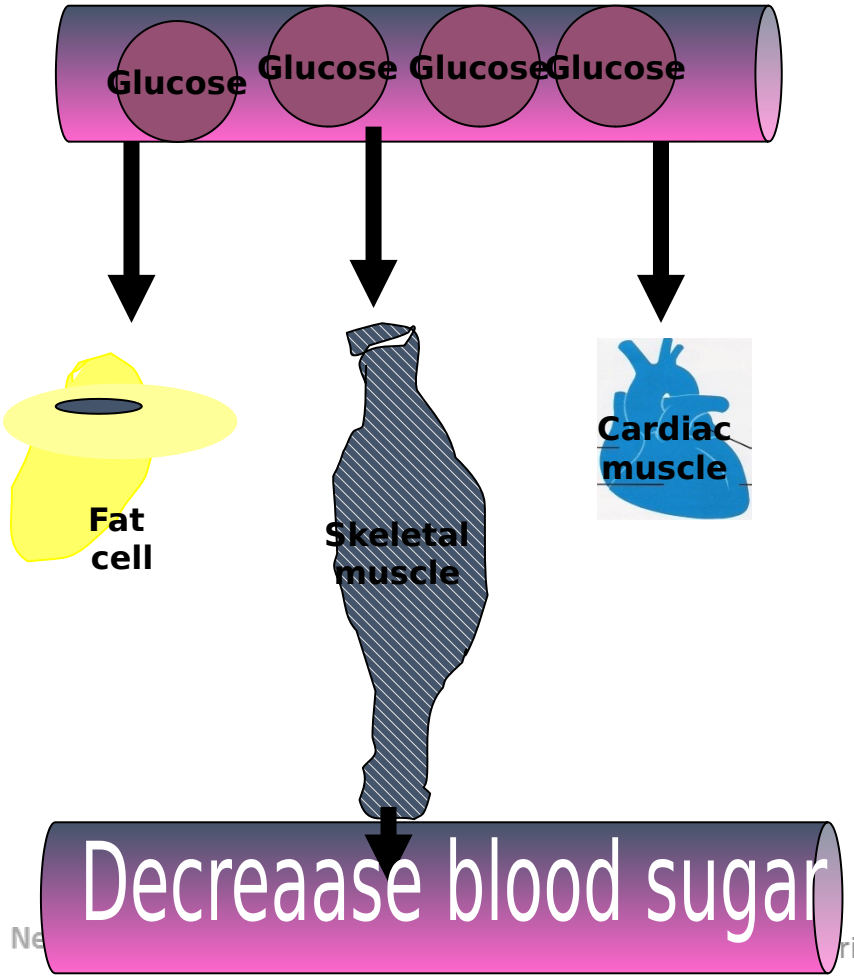
↑ Glucagon Secretion	↓ Glucagon Secretion
1.Hypoglycemia 2. Amino acids 3. Gastrin &CCK 4. Exercise 5. Stress 6. β adrenergic stimulants 7. Acetylcholine	1. Glucose 2. FFA, Ketones 3.Secretin 4.Somatostatin & Insulin 5. adrenergic stimulants

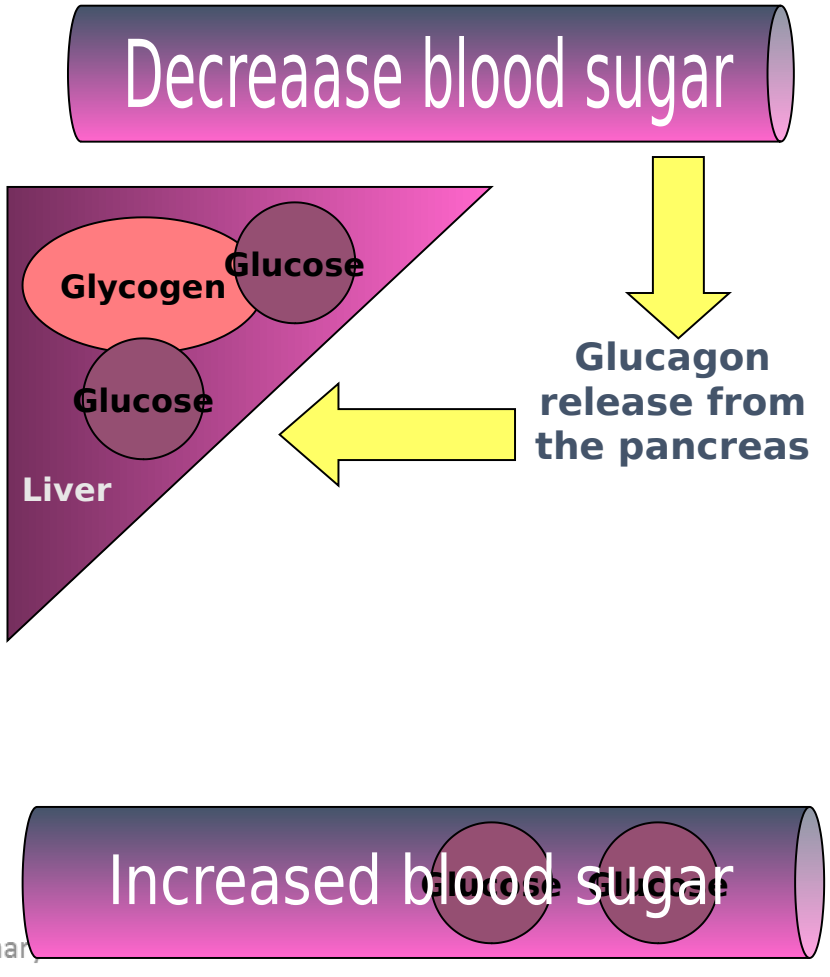
After meals

During fasting

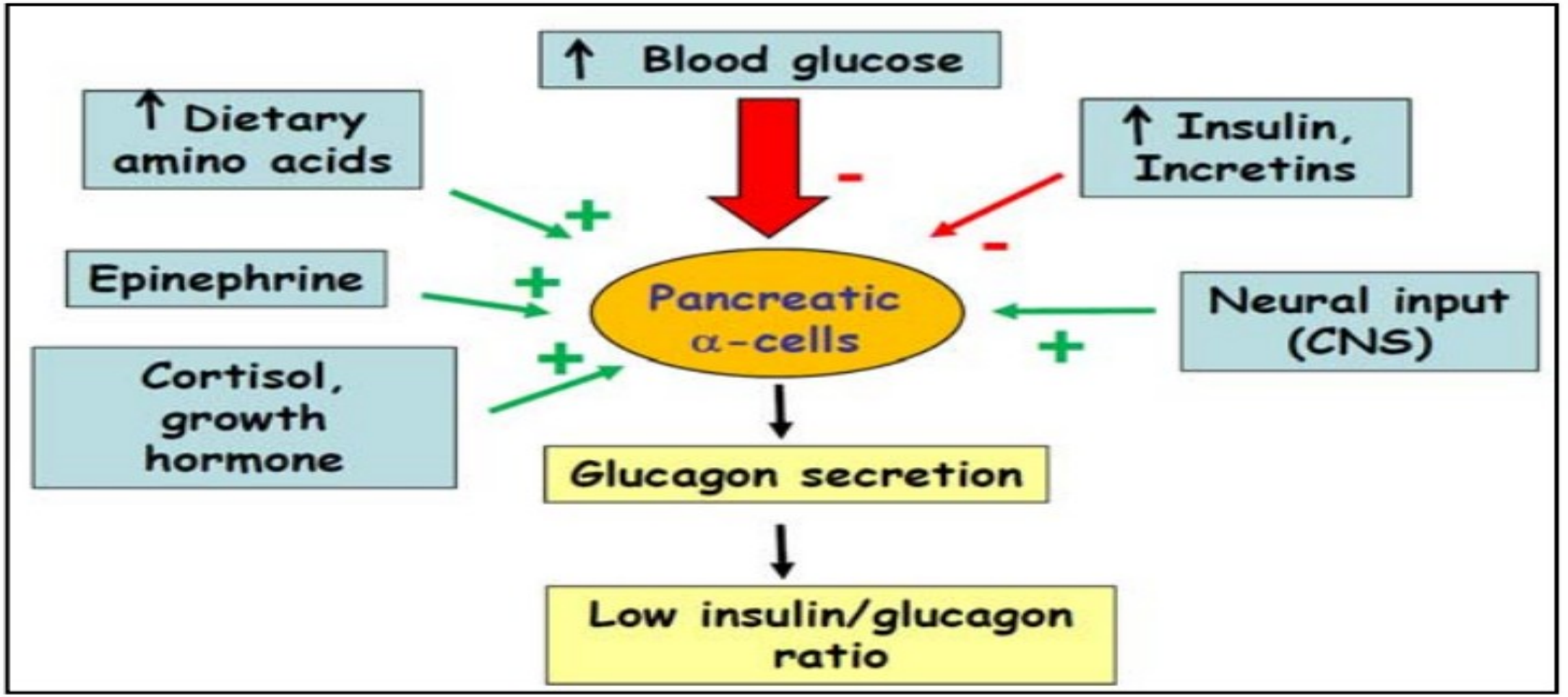


Glucagon





Regulation of glucagon secretion



https://www.memorangapp.com/flashcards/60350/L28_InsulinandGlucagon/

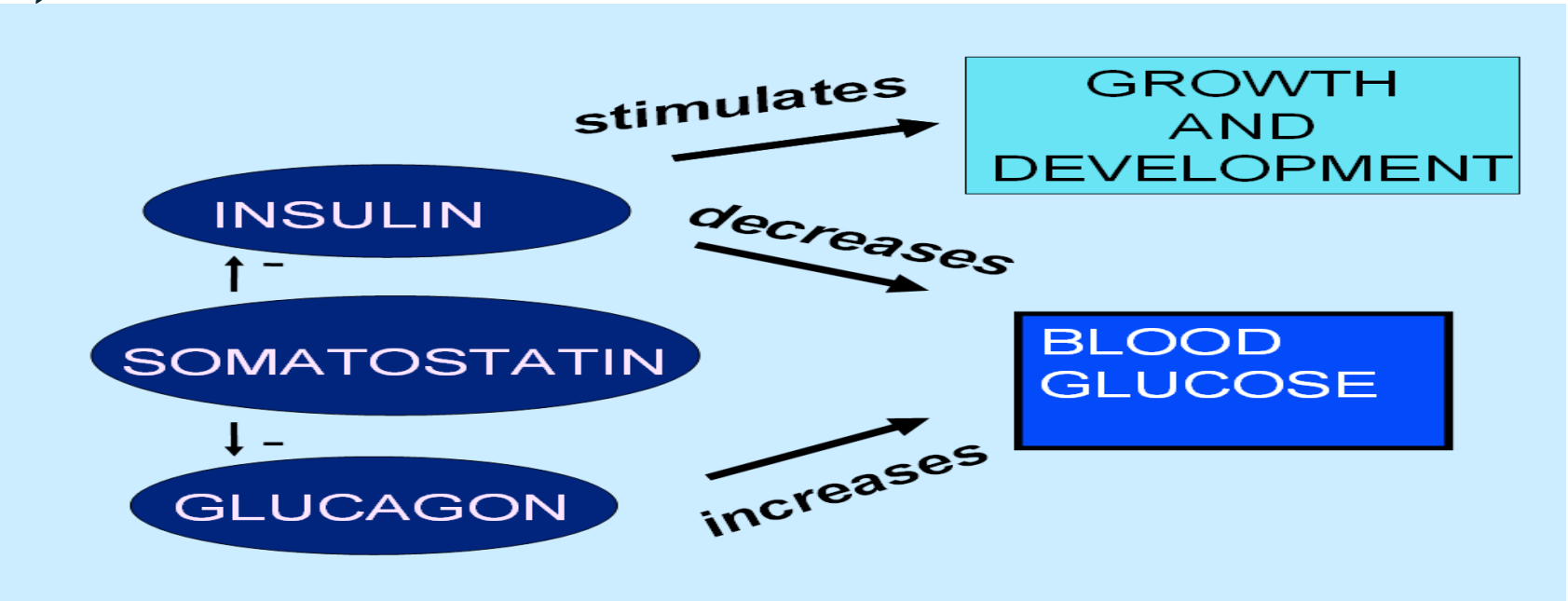
Somatostatin Hormone

- **Site of release:** Delta-cells of pancreas, intestinal mucosa and hypothalamus.
- **Physiological actions:**

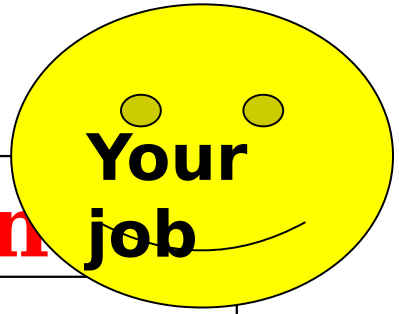
1- (-) both insulin and glucagon.

(acts locally in a paracrine way pancreatic islets secretion)

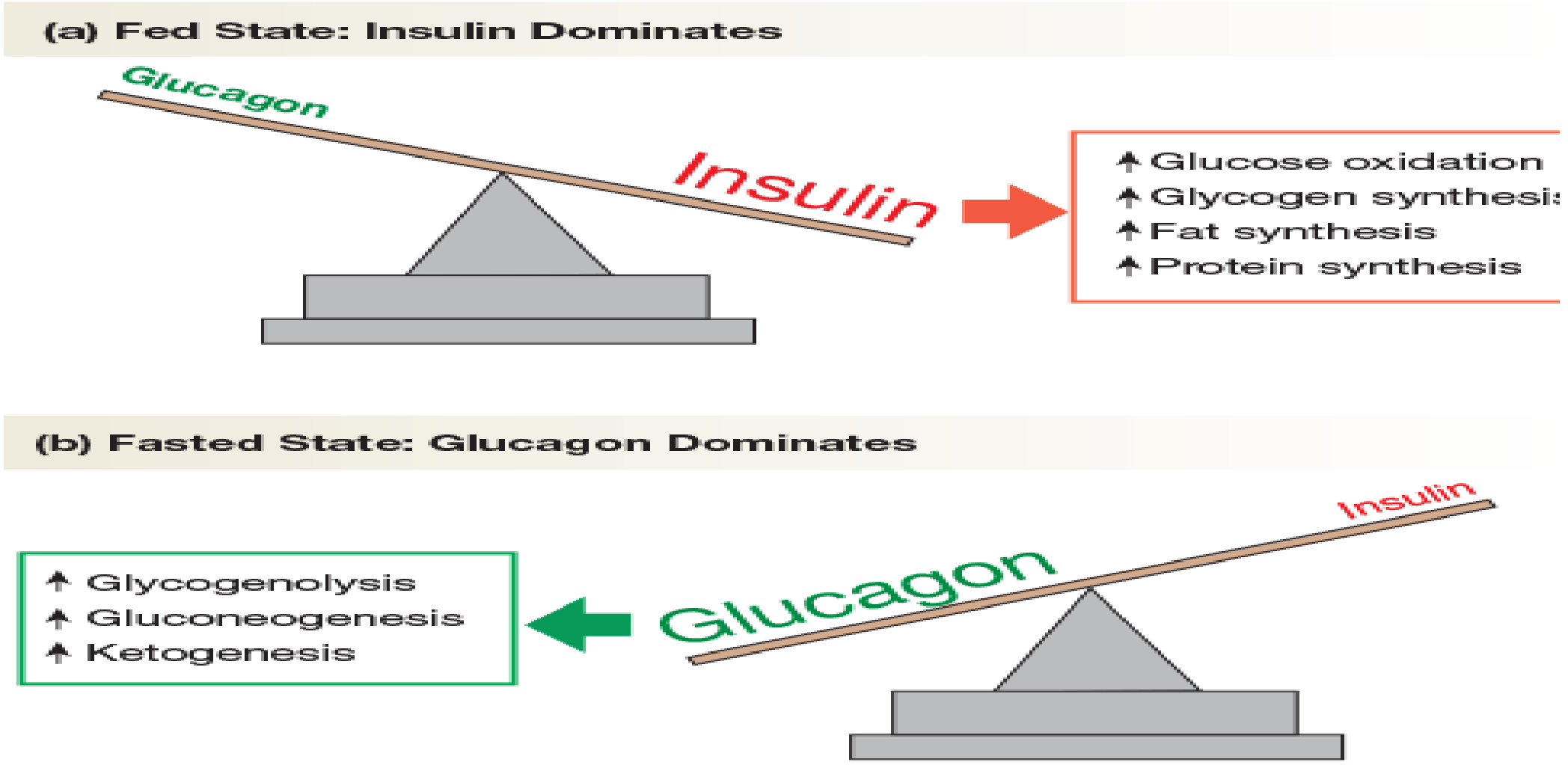
2- (-) G



Insulin vs Glucagon (Compare?)



	Insulin	Glucagon
Site of release	Beta cells …	Alpha cells…
Nature:	Peptide hr(51 a.a)	Peptide hr (29 a.a)
Mechanism of action:	(+) the tyrosine kinase activity of β subunit autophosphorylation……	via G protein coupled receptors cAMP
Actions: **CHO** **Lipid** **Protein**	Hypoglycemic Lipogenic Anti-ketotic Anabolic	Hyperglycemic Lipolytic Ketogenetic Catabolic
	Hr. of energy store	Hr. of energy release
Stimulators	… bl.glucose, a.a, GIT hrs	↓ Bl.glucose, a.a, B agonists…
Inhibitors	…blood glucose & SS↓	bl. Glucose, SS…
Its deficiency	Diabetes mellitus	Hypoglycaemia



https://bodyexpertsystems.com/the-fat-burning-switch-insulin-vs-glucagon/

Hormones Regulating Glucose Metabolism

- The blood glucose level is regulated by a balance between insulin ***(hypoglycemic)*** and insulin antagonist ***(hyperglycemic)*** hormones.

Anti-insulin hormones (hyperglycemic hormones):

1- Glucagon.

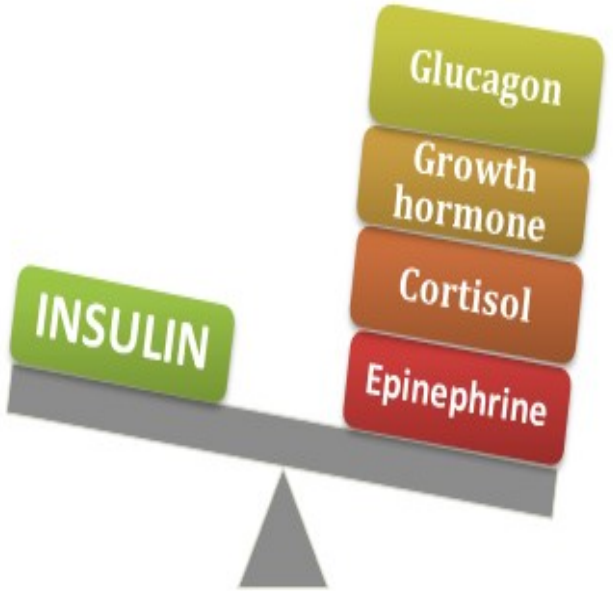
2- Epinephrine.

3- Cortisol.

4- Growth hormone.

5- Thyroid hormone.

 they are important during hypoglycemia.



http://howmed.net/pathology/hormones-regulating-carbohydrate-me

Hormones Regulating Glucose Metabolism

Glucagon

- 1- (+) hepatic glycogenolysis.
- 2- (+) hepatic gluconeogenesis.
- 3- (-) glycogen synthesis.

Epinephrine

1- (-) insulin secretion & (+) glucagon

2- (+) glycogenolysis in liver & muscles.

3- ↓ glucose uptake by the muscles.

Glucocorticoids

1- (-) insulin and (+) glucagon & epinephrine.

2- ↓ glucose uptake by the adipose tissue.

3 - (+) hepatic gluconeogenesis

- Lipolysis in adipose tissue (glycerol for gluconeogenesis)
- Breakdown of proteins (catabolic hormone) amino acids for gluconeogenesis).

Hormones Regulating Glucose Metabolism

Growth hormone

1- Decrease glucose uptake.

2- Decrease the number of insulin receptors.

3- (+) hepatic gluconeogenesis

Thyroid Hormones

1- ↑ glucose absorption from GIT.

2- (+) gluconeogensis.

3- (+) glycogenolysis.

Lecture Quiz

Q1. Which of the following is true about pancreatic glucagon?

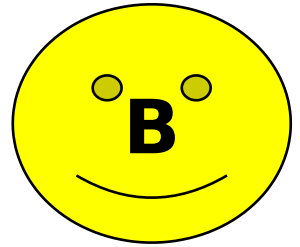
a. Is a major hypoglycemic factor.

b. Increases gluconeogensis in liver.

c. Increases glycogenolysis in muscles.

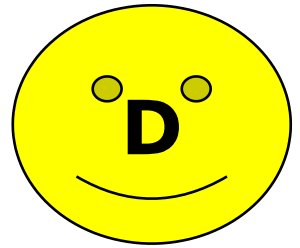
d. Decreases the cAMP._

e. Is a hormone of energy store.



Lecture Quiz

Q2. Insulin secretion from β cells of pancreas is stimulated by:



a. Somatostatin.

b. Atropine.

c. Activation of α-adrenergic receptors.

d. GIP.

e. Leptin.

SUGGESTED TEXTBOOKS

1. **Guyton and Hall Textbook of Medical Physiology.**
   https://www.amazon.com/Guyton-Hall-Textbook-Medical-Physiology/dp/1455770051

2. **Ganong's Review of Medical Physiology, 25e. Chapter 21, pages (315 to 335)**

   https://www.amazon.com/Ganongs-Review-Medical-Physiology-Twenty-Fifth/dp/007182510X


Thank You
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